

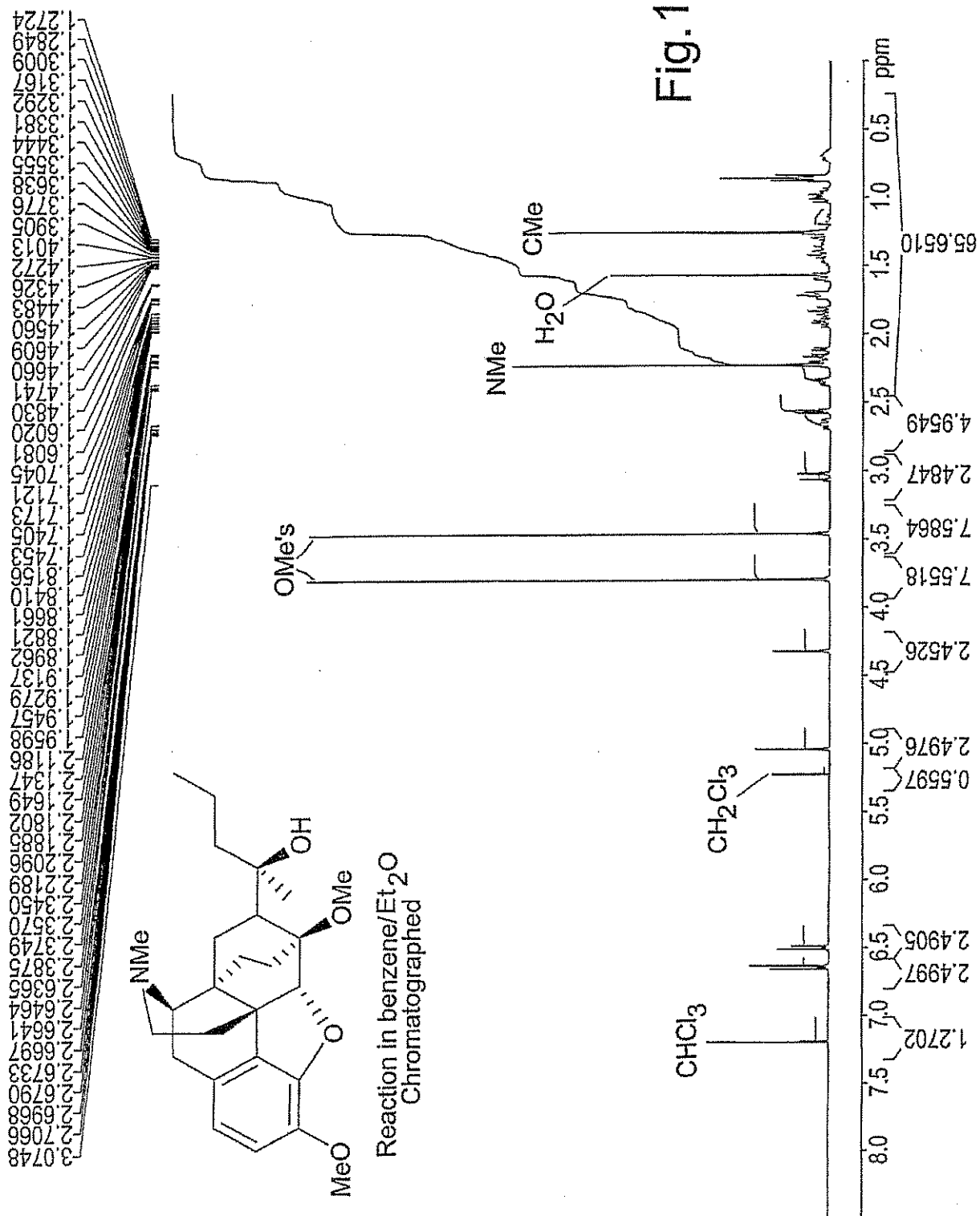
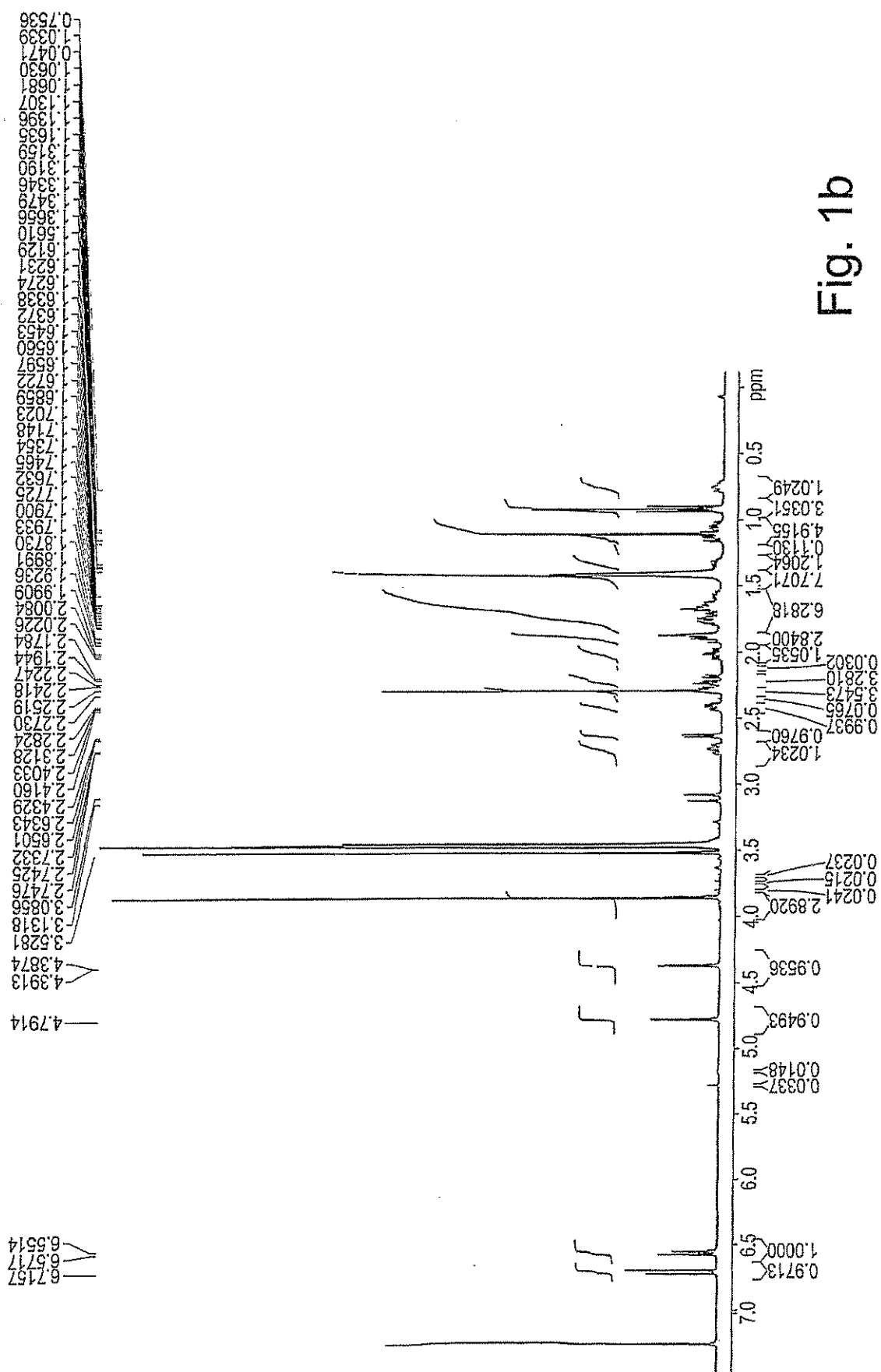
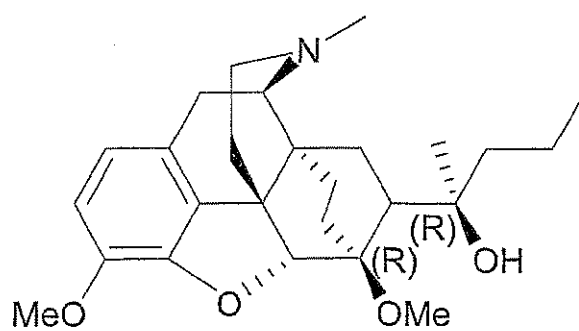
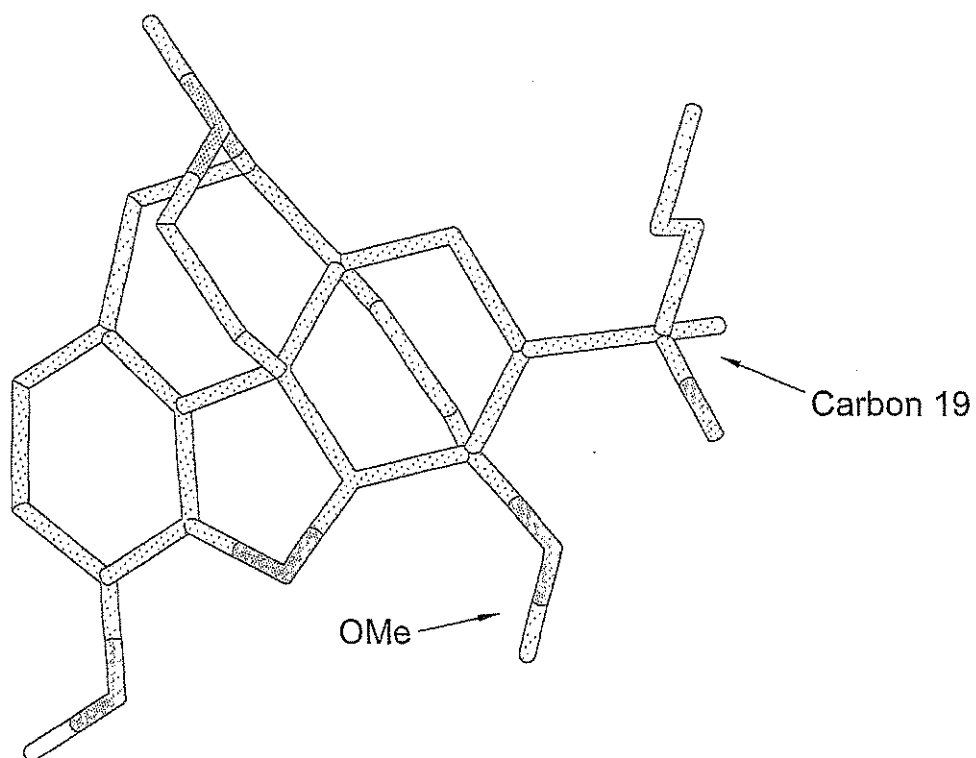


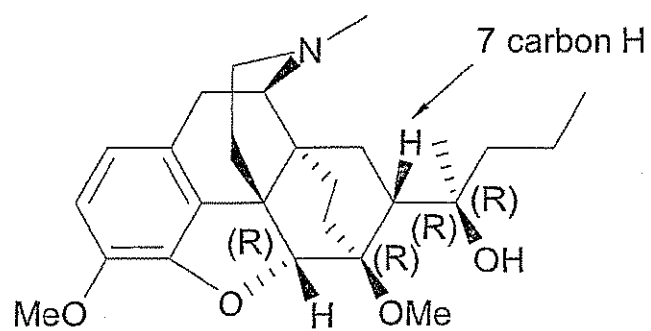
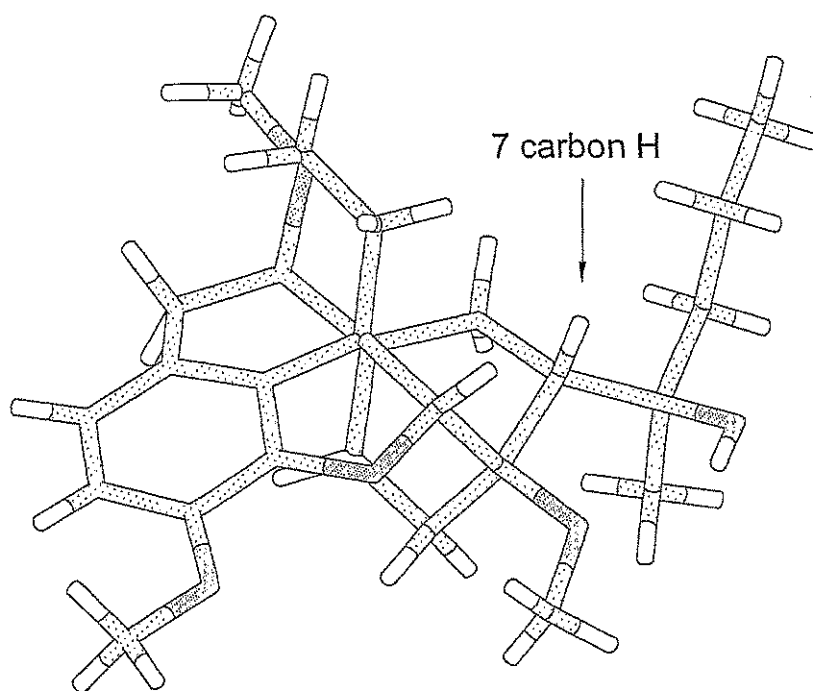
Fig.1a





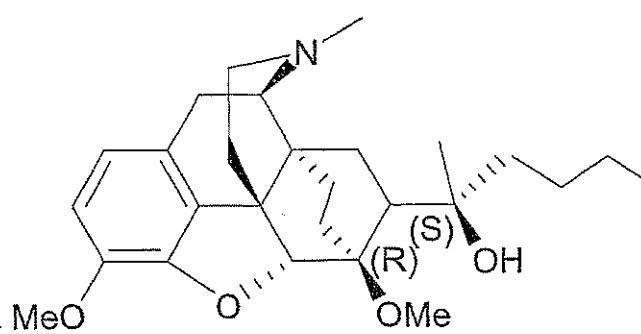
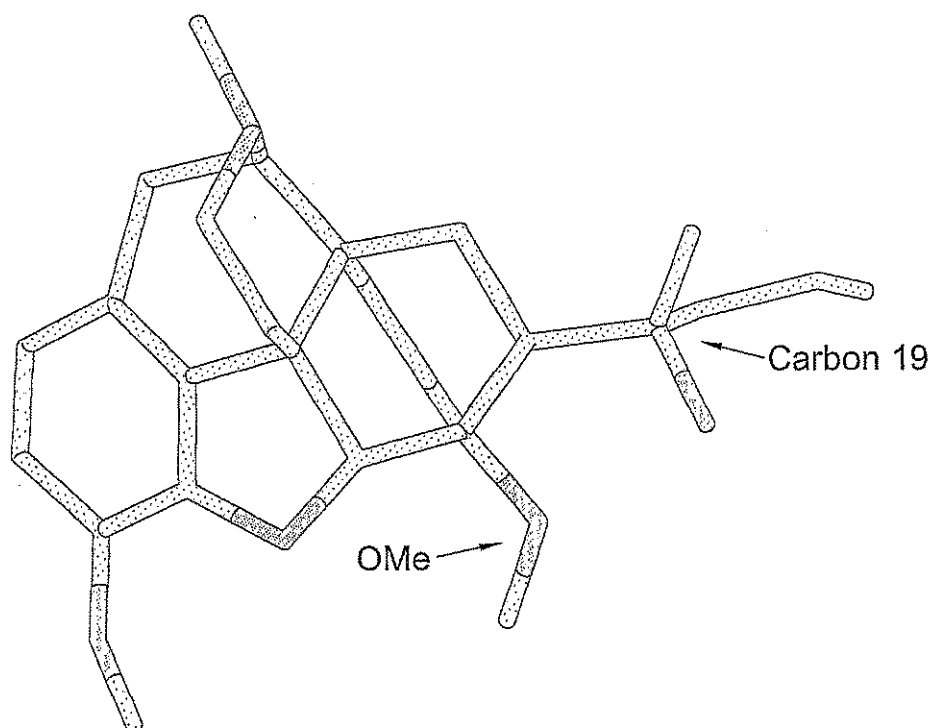
(R)-19-Pr-DHT

Fig. 2



(R)-19-Pr-DHT

Fig. 3



(S)-19-Pr-DHT

Fig. 4

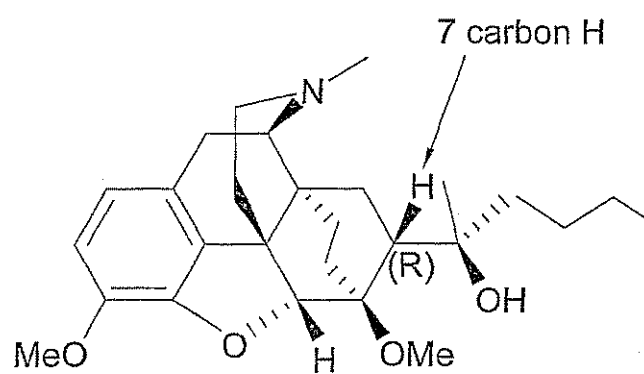
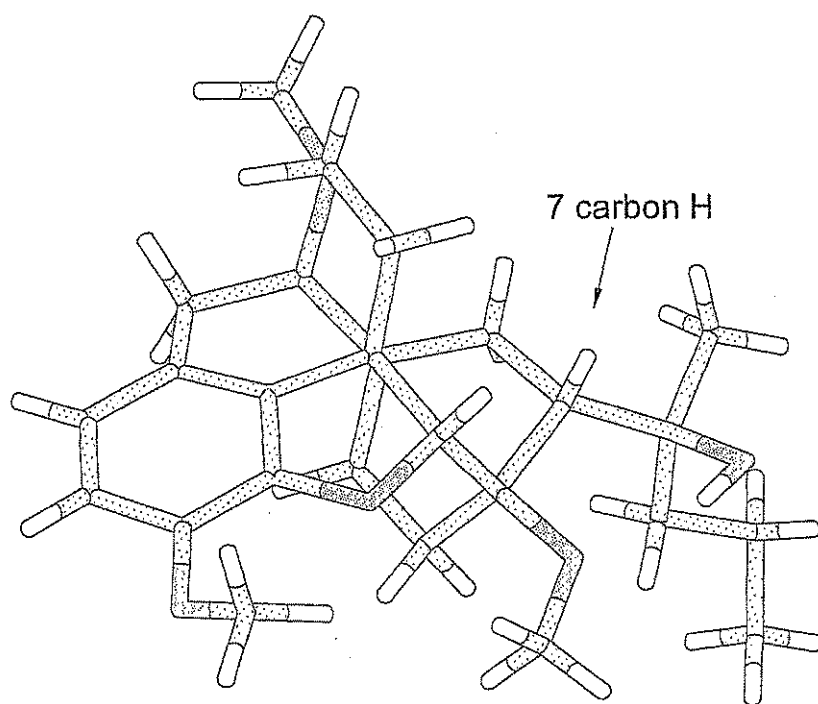


Fig. 5

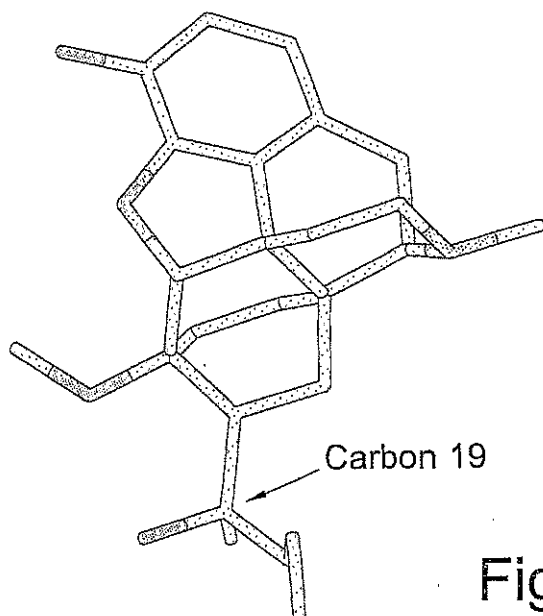


Fig. 6

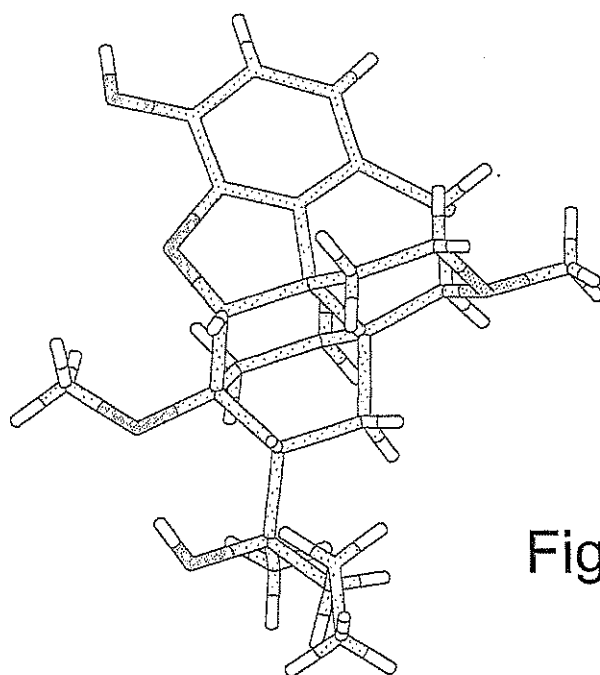


Fig. 7

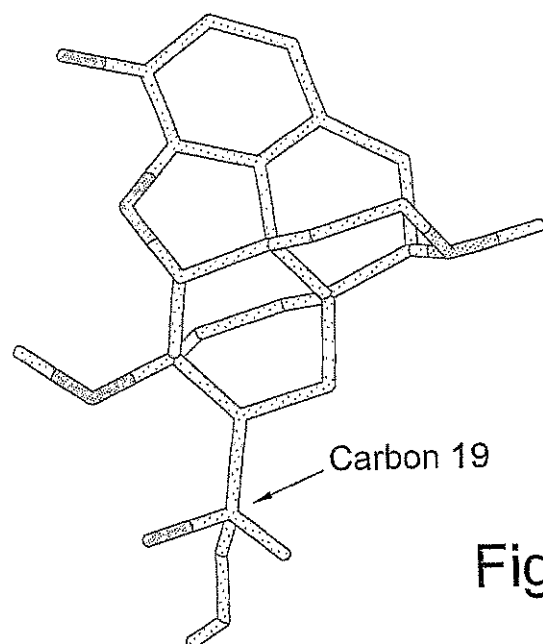


Fig. 8

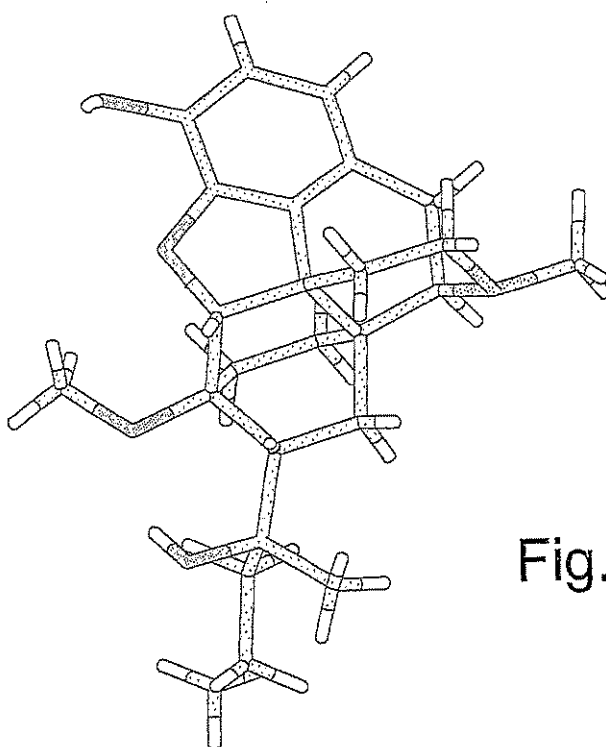


Fig. 9

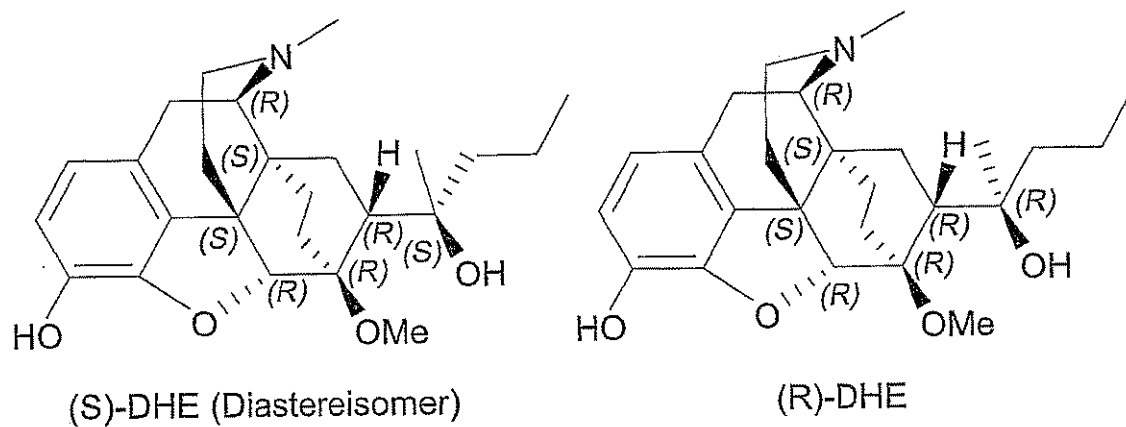
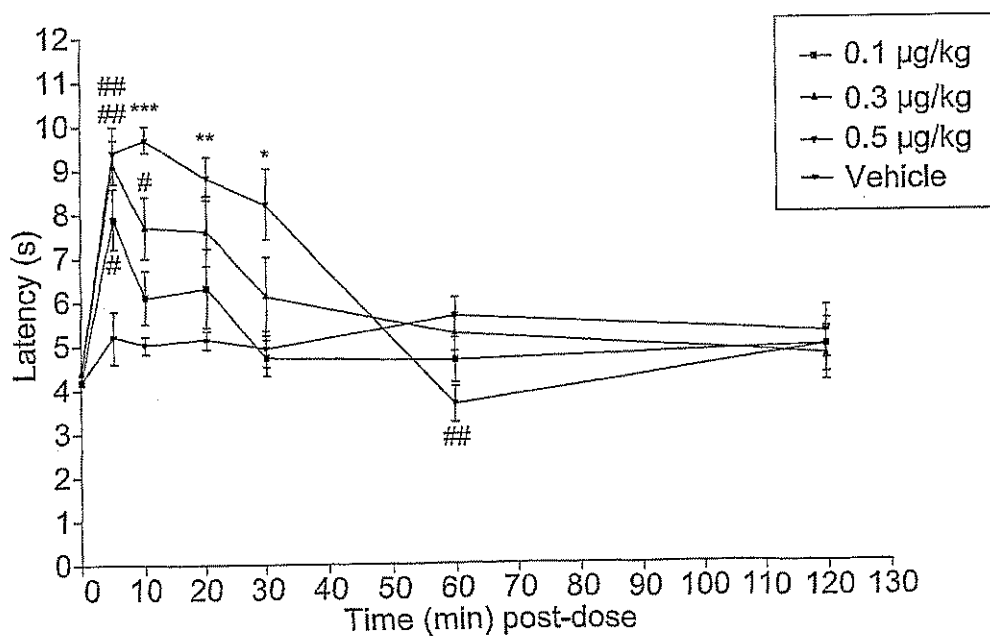


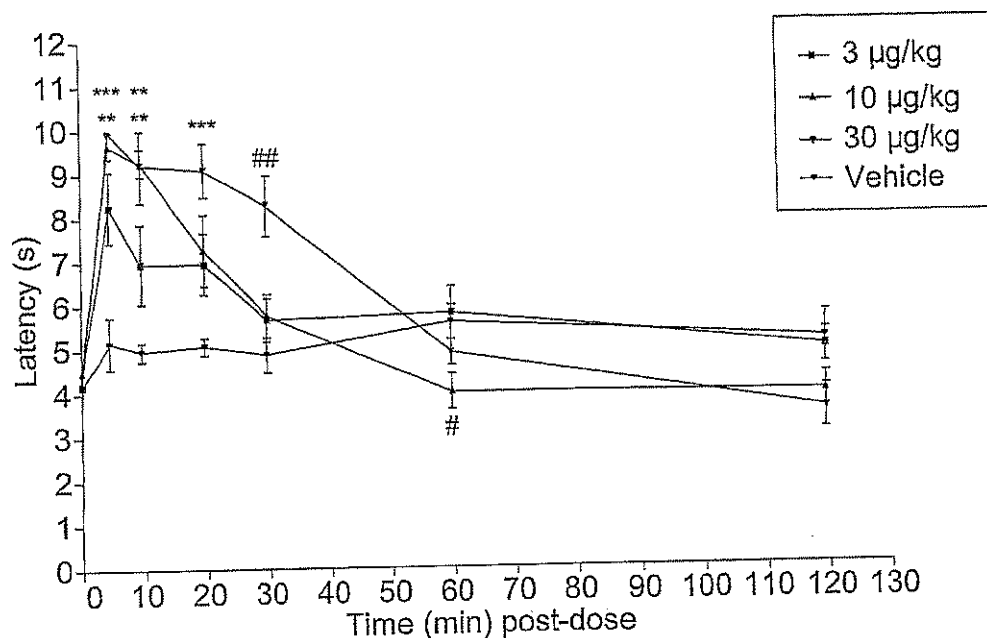
Fig. 10



$P < 0.05$, ## $P < 0.01$ when compared to vehicle (ANOVA and Dunnett's t-test).
 * $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$ when compared to vehicle (Kruskal-Wallis and Dunn's test).

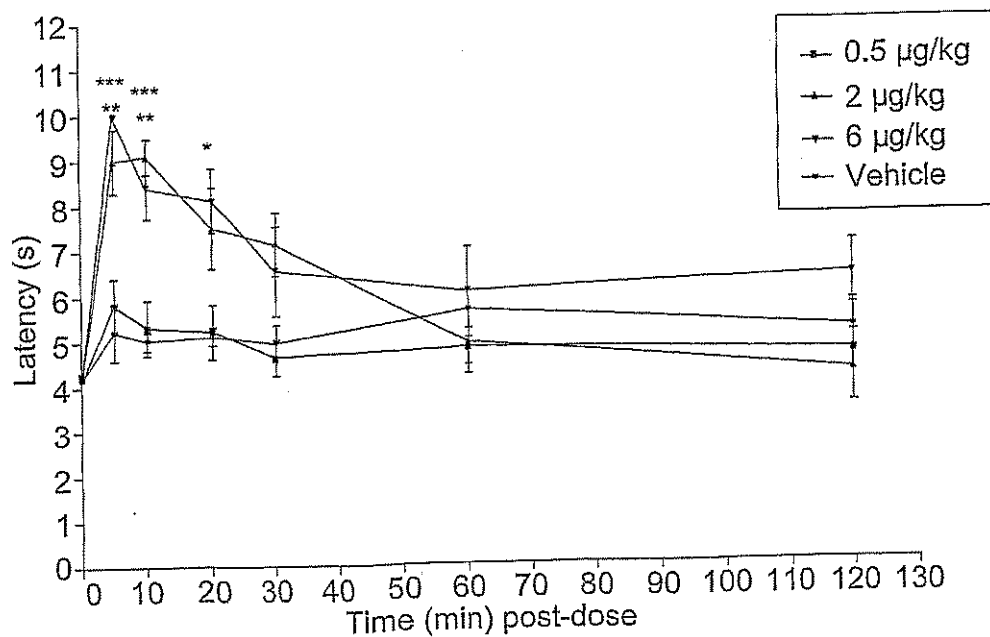
Fig. 11

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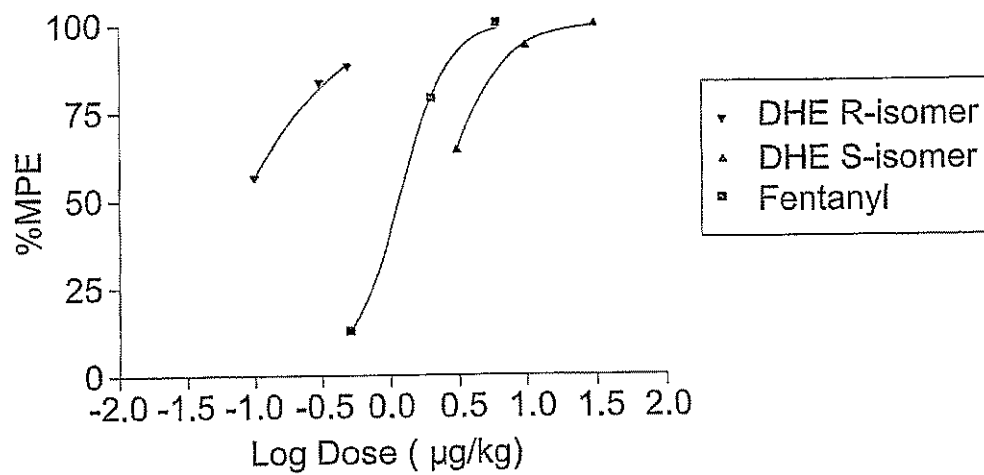
$P < 0.05$, ## $P < 0.01$ when compared to vehicle (ANOVA and Dunnett's t-test).
 ** $P < 0.01$ and *** $P < 0.001$ when compared to vehicle (Kruskal-Wallis and Dunn's test).

Fig. 12



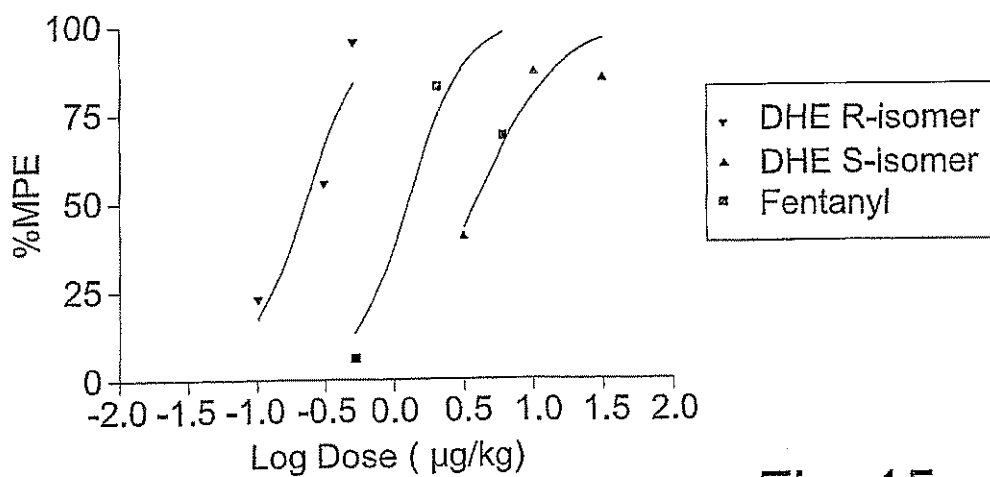
* $P < 0.05$ and ** $P < 0.01$ and *** $P < 0.001$ when compared to vehicle (Kruskal-Wallis and Dunn's test).

Fig. 13



DHE R-isomer ED₅₀=0.07914 µg/kg
DHE S-isomer ED₅₀=2.165 µg/kg
Fentanyl ED₅₀=1.135 µg/kg

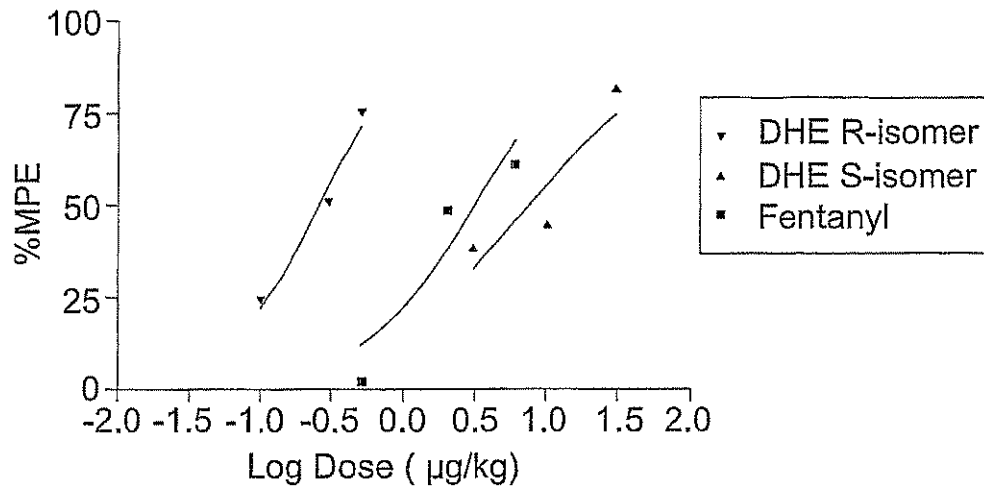
Fig. 14



DHE R-isomer ED₅₀=0.2253 µg/kg
DHE S-isomer ED₅₀=3.795 µg/kg
Fentanyl ED₅₀=1.239 µg/kg

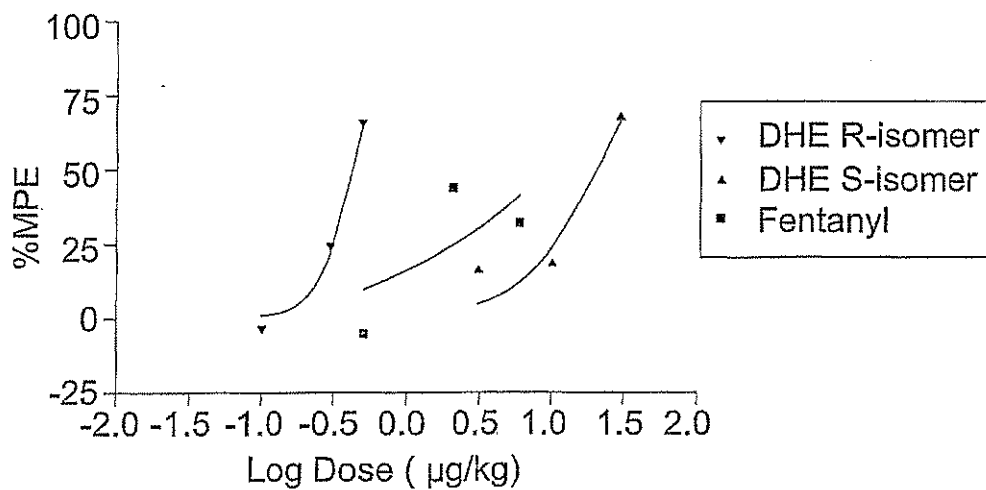
Fig. 15

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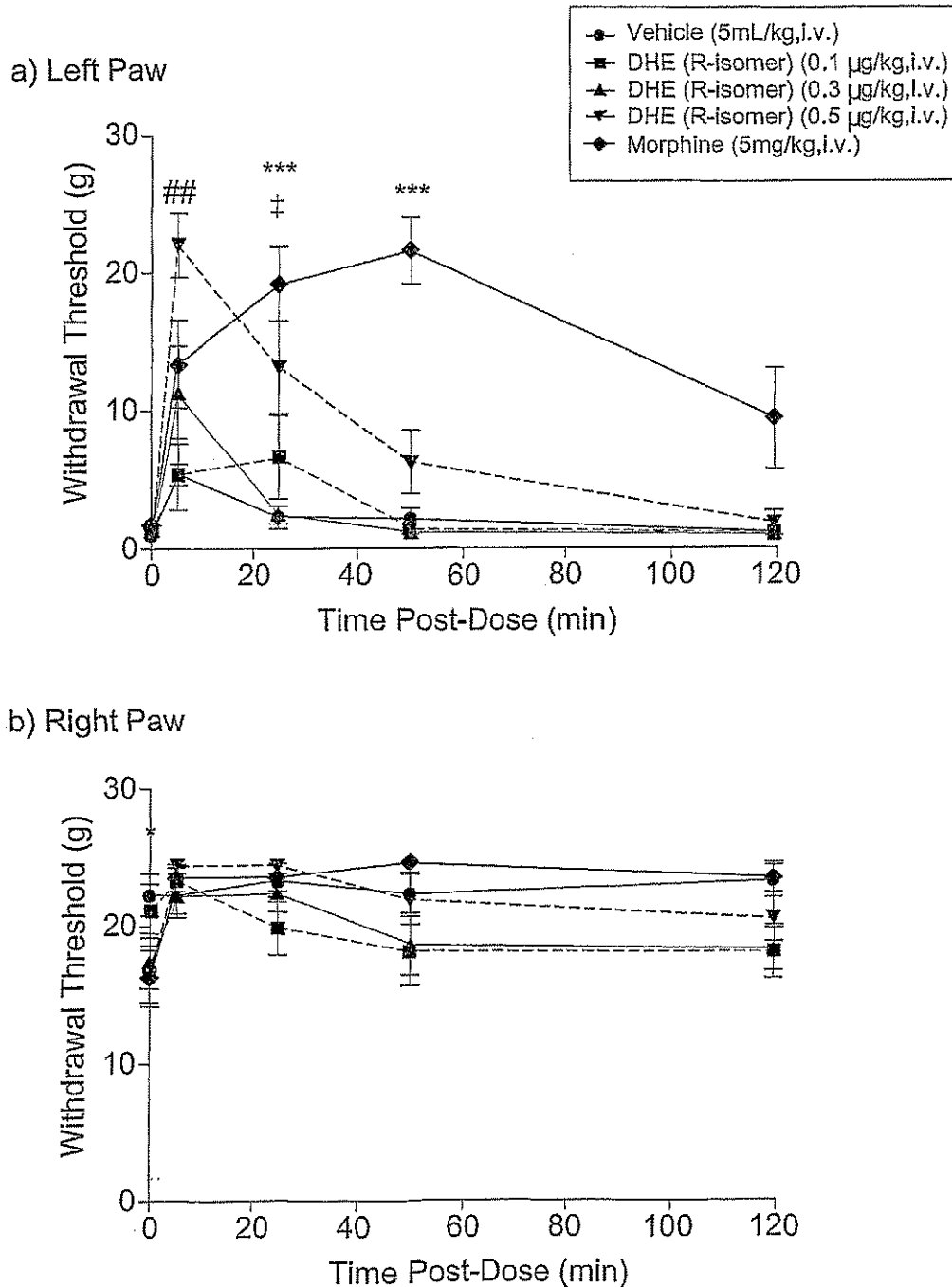
DHE R-isomer ED₅₀=0.2532 µg/kg
DHE S-isomer ED₅₀=7.516 µg/kg
Fentanyl ED₅₀=3.111 µg/kg

Fig. 16



DHE R-isomer ED₅₀=0.4222 µg/kg
DHE S-isomer ED₅₀=20.95 µg/kg
Fentanyl ED₅₀=9.681 µg/kg

Fig. 17

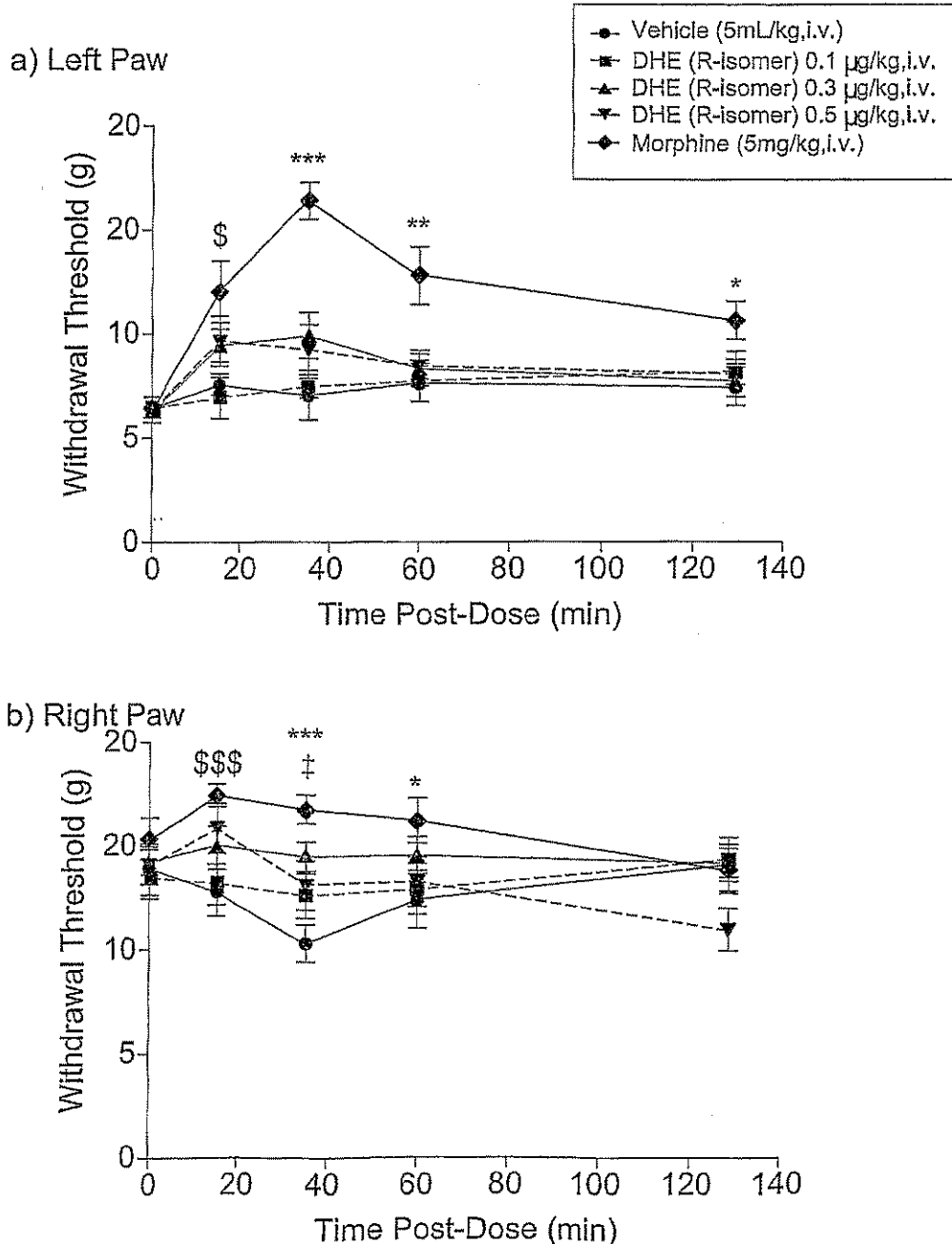


##P<0.01 when compared to vehicle group data(Kruskal-Wallis and Dunn's test)

‡ P < 0.05 when compared to vehicle group data (ANOVA and Dunnett's t-test).

* P < 0.05, *** P < 0.001 when compared to vehicle group data (Unpaired 2-tailed Student's t-test).

Fig. 18



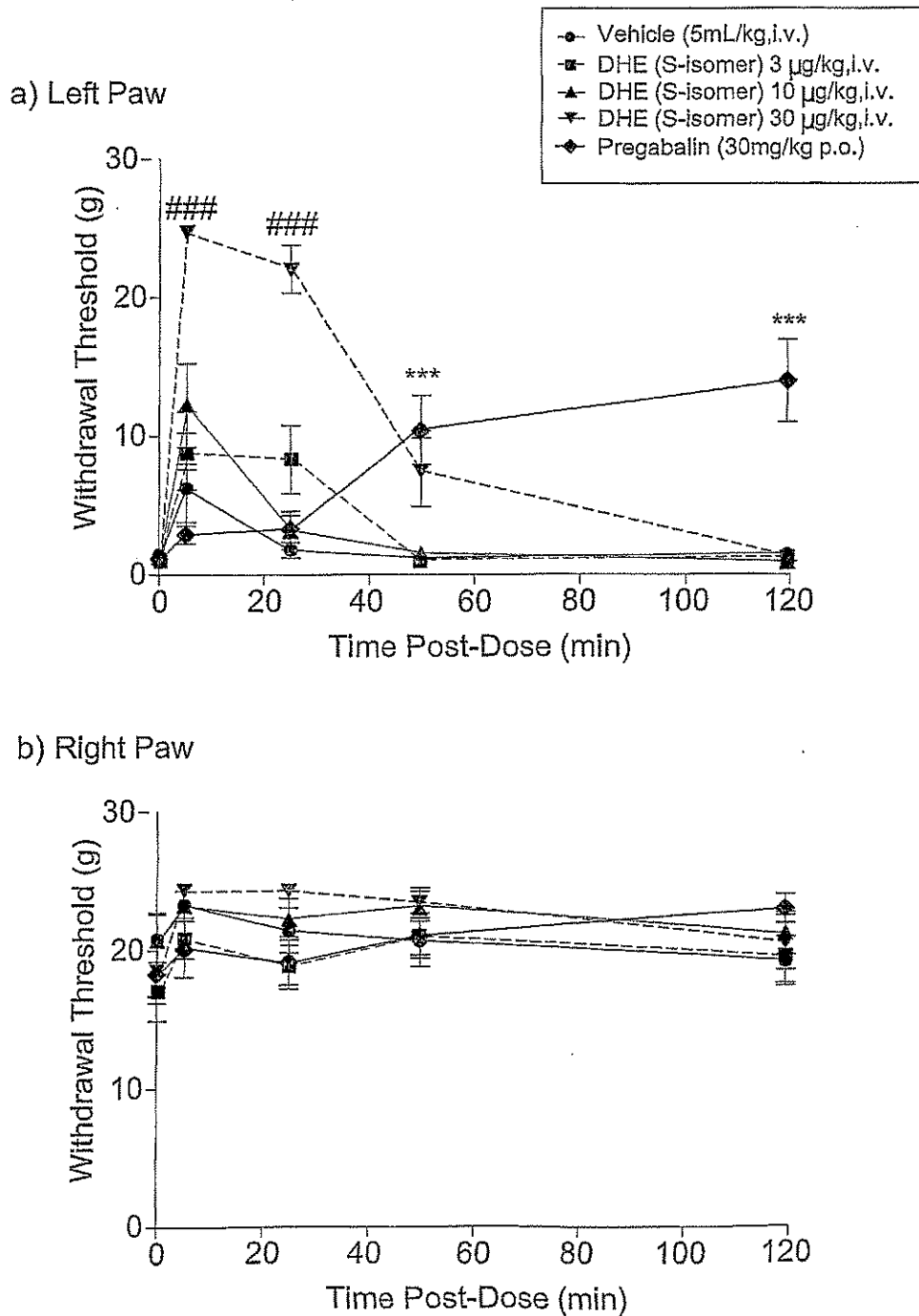
\$P < 0.05, \$\$\$ P < 0.001 when compared to vehicle group data (Mann-Whitney U-test).

when compared to vehicle group data (unpaired 2-tailed Student's t-test).

* P < 0.05, ** P < 0.01, *** P < 0.001 when compared to vehicle group data (unpaired 2-tailed Student's t-test).

‡ P < 0.05 when compared to vehicle group data (ANOVA and Dunnett's t-test).

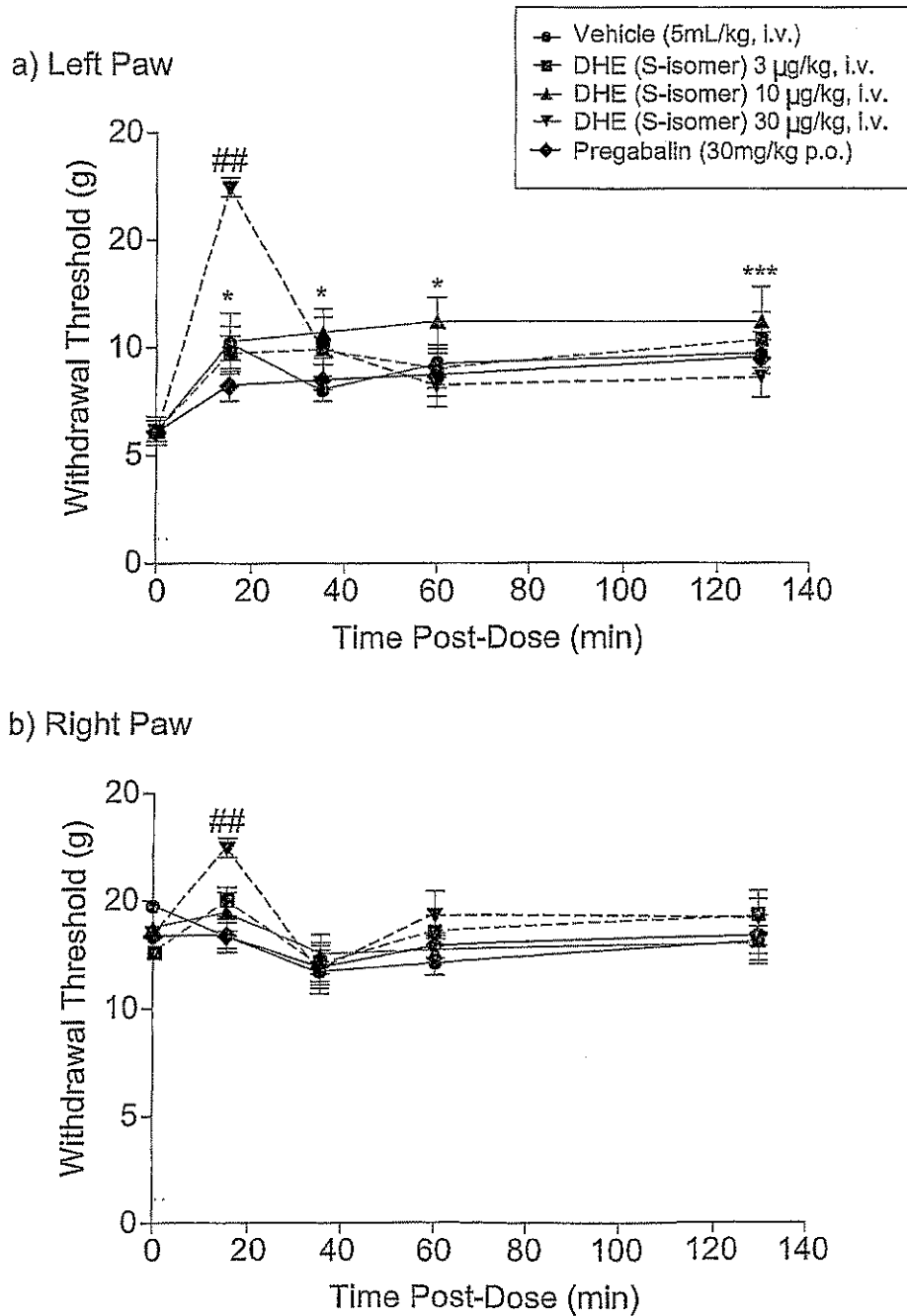
Fig. 19



*** $P < 0.001$ when compared to pre-dose data (paired 2-tailed Student's *t*-test).

$P < 0.001$ when compared to vehicle group data (Kruskal-Wallis and Dunn's test).

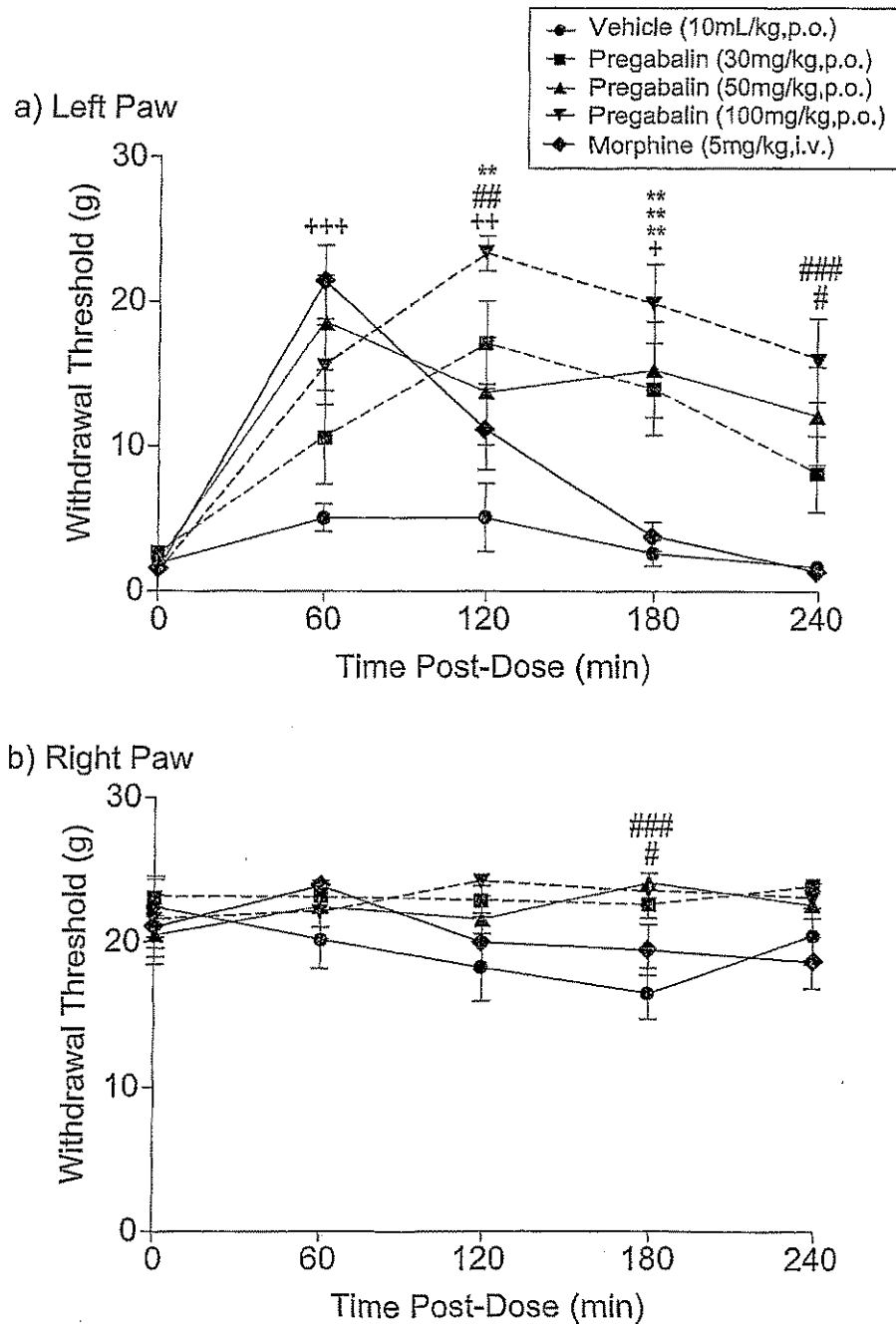
Fig. 20



$P < 0.01$ when compared to vehicle group data (Kruskal-Wallis and Dunn's test).

* $P < 0.05$, *** $P < 0.001$ when compared to pre-dose data (paired 2-tailed Student's t-test).

Fig. 21



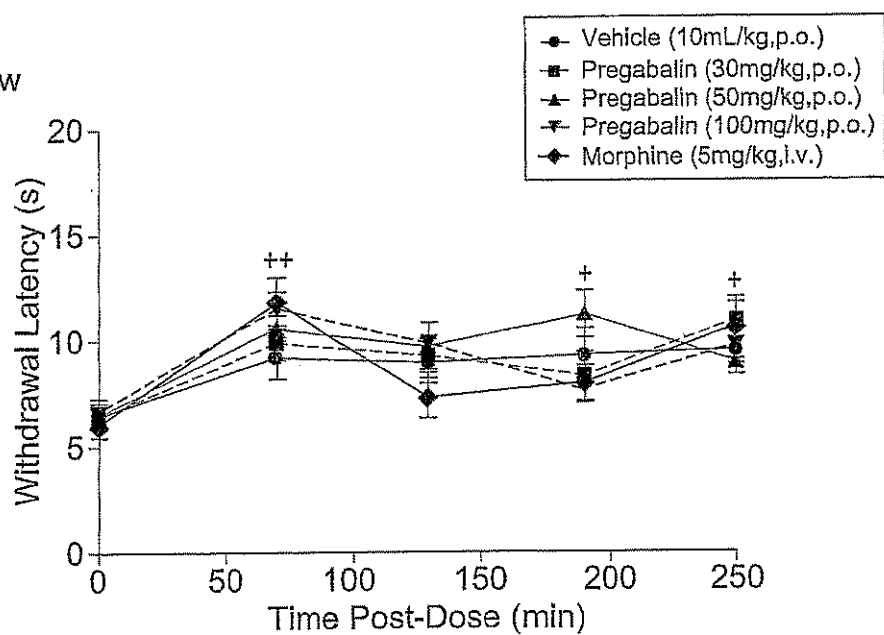
+ $P < 0.05$, ++ $P < 0.01$ and +++ $P < 0.001$ when compared to pre-dose data (paired 2-tailed Student's t-test).

$P < 0.05$, ## $P < 0.01$ and ### $P < 0.001$ when compared to vehicle group data (Kruskal-Wallis and Dunn's test).

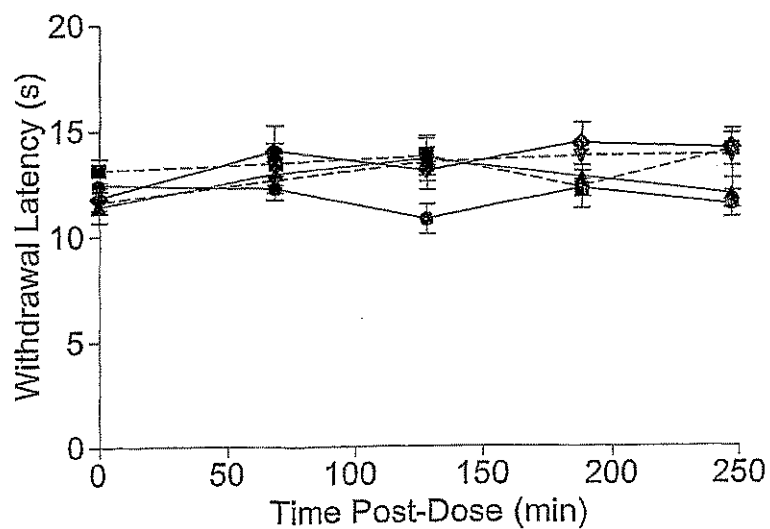
** $P < 0.01$ when compared to vehicle group data (ANOVA and Dunnett's test).

Fig. 22

a) Left Paw



a) Right Paw



+ $P < 0.05$, ++ $P < 0.01$ when compared to pre-dose data (paired 2-tailed Student's t-test).

Fig. 23